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EXAMINER	
FISHER, ABIGAIL L	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,990	SCHACHT ET AL.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,10-13 and 15-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10-13 and 15-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/27/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Remarks filed on October 27 2010 is acknowledged. Claims 3-9 and 14 were/stand cancelled. Claim 25 was amended. Claims **1-2, 10-13 and 15-25** are pending.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on October 27 2010 was considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.

3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 10-11 and 17-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (US Patent No. 5788983, cited in the Office action mailed on 10627990) in view of Gale et al. (US Patent No. 4588580, cited in the Office action mailed on 4/27/10).

Applicant Claims

The instant application claims a transdermal delivery system comprising, a self adhesive matrix containing a self-adhesive polymer and microreservoirs containing an amine-functional drug in free base form selected from the group consisting of fentanyl and oxybutynin wherein the microreservoirs are within the self-adhesive matrix and have a maximum diameter less than the thickness of the self-adhesive matrix; and wherein the self-adhesive matrix is permeable to the amine functional drug in free base

form and the self adhesive matrix is substantially impermeable to the amine functional drug in protonated form.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Chien et al. is directed to transdermal controlled delivery of pharmaceuticals at variable dosage rates and processes. The transdermal dosage unit for administration of one or more pharmaceuticals at controlled and variable rates comprises a backing layer which is impervious to the ingredients of the dosage unit, a reservoir having present for transdermal absorption, a means which desirably provide variable transdermal absorption rates and an adhesive means to affix the dosage unit to the skin (column 2, lines 28-48). It is taught that if the at least one pharmaceutical is to be present in the reservoir in the form of microreservoirs of the pharmaceutical, the pharmaceutical can be dissolved in a biocompatible liquid which can provide variability of transdermal absorption. The pharmaceutical can be dissolved or dispersed in the liquid before dispersion into a biocompatible polymeric material, such as an adhesive polymer and then stirred at sufficiently high speed to form a pharmaceutical containing polymeric material **wherein microreservoirs of the dissolved pharmaceutical are dispersed in a polymeric material** (column 4, lines 1-16). The backing layer can be made of any suitable material which is impermeable to the pharmaceutical dispersed within the adjacent reservoir layer (column 6, lines 33-35). Examples include a laminate of aluminum foil and polyester film (column 6, lines 64-66). The polymer material selected must permit the pharmaceutical to be released for the desired transdermal absorption

and not substantially affect the pharmaceutical component or the permeability regulating membrane or other components. The reservoir medium containing dissolved/dispersed pharmaceutical and the polymeric material are combined in a suitable amount and agitated using suitable stirring or dispersing means to cause microreservoirs to be formed and homogeneously dispersed in the polymeric material. It is normally desired that the microreservoirs be of micronic diameter such as 2 to about 200 microns, usually preferably about 5 to 100 microns in diameter (column 9, lines 25-27). The adhesive polymer used can be selected from known adhesives which are bioaccecptable and pressure sensitive (column 9, lines 28-40). The dosage units can vary in surface area and shape as desired (column 9, lines 50-57). A wide variety of pharmaceuticals are taught as being suitable. These include morphine and other narcotic analgesics. However, it is stated that it is contemplated that any pharmaceutical can be utilized by this invention (column 11, lines 14-63).

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

While Chien et al. teach that any pharmaceutical can be utilized; Chien et al. do not teach that the pharmaceutical is fentanyl. While Chien et al. teach that the polymer in which the pharmaceutical microreservoirs can be dispersed include adhesives, Chien et al. do not specify that the adhesive is a silicone adhesive. However, these deficiencies are cured by Gale et al.

Gale et al. is directed to transdermal administration of fentanyl. Fentanyl is a well known potent and effective anesthetic and analgesic (column 1, lines 13-16). It is

taught that fentanyl citrate, the form it is typically administered, has such low skin permeability that it is not suitable for transdermal delivery even with the use of permeation enhancers. Therefore, the preferred form of fentanyl for transdermal delivery is the base form of the drug (column 3, lines 9-16). Example 6 is directed to a monolithic system fabricated using Dow Corning amine resistant silicone adhesive and fentanyl base dispersed therein.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Chien et al. and Gale et al. and utilize fentanyl base as the pharmaceutical agent. One of ordinary skill in the art would have been motivated to utilize fentanyl base as Chien et al. teach that analgesics can be administered and that pretty much any pharmaceutical agent can be delivered. Gale et al. teach that fentanyl base can be delivered transdermally to produce an analgesic effect. Therefore, one of ordinary skill in the art would have been motivated to utilize fentanyl base when desiring to deliver an analgesic transdermally. Further more, the selection of a specific drug is considered prima facie obvious depending on the desired condition/symptoms to be treated.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Chien et al. and Gale et al. and utilize silicone adhesives. One of ordinary skill in the art would have been motivated to utilize silicone adhesives as Chien et al. teach that the adhesive polymer used can be selected

from known adhesives which are bioacceptable and pressure sensitive. Gale et al. exemplify utilizing amine resistant silicone adhesives with fentanyl dispersed therein. Therefore, one of ordinary skill in the art would have been motivated to utilize silicone adhesives as they are a known adhesive suitable for use with fentanyl base. The prior art teaches the use of fentanyl with silicone adhesives. Therefore, all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. **Note: MPEP 2141 [R-6]** *KSR International CO. v. Teleflex Inc.* 82 USPQ 2d 1385 (Supreme Court 2007).

Regarding the claimed limitation that the maximum diameter is less than the thickness of the self-adhesive matrix, it is taught that the microreservoirs are dispersed in the polymeric adhesive. Since they are dispersed therein, their corresponding diameter would be less than the thickness of the adhesive matrix. Furthermore, the method of making the microreservoirs are substantially similar to the method taught in the instant specification.

Regarding the claimed diameter of the microreservoirs, Chien et al. teach an amount that overlaps that instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]**

Regarding the claimed number of microreservoirs, Chien et al. is silent. However, the surface area of the transdermal device overlaps that taught in the

specification, the method of making the reservoirs is substantially similar to the method taught in the specification. Furthermore, since the number of reservoirs is related to the amount of pharmaceutical present, it would have been obvious to one of ordinary skill in the art to vary the number of reservoirs depending on the desired amount of drug to be administered. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. It would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).

Regarding instant claim 10, Chien et al. does not teach the addition of silica particles therefore there is a reasonable expectation that the self-adhesive matrix is free of silica particles.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. in view of Muller et al. (WO 99/49852, cited on PTO Form 1449).

Applicant Claims

The instant application claims a transdermal delivery system comprising a self adhesive matrix containing a self-adhesive polymer and microreservoirs containing an amine-functional drug selected from an aminotetraline compound wherein the microreservoirs are within the self-adhesive matrix and have a maximum diameter less than the thickness of the self-adhesive matrix; and wherein the self-adhesive matrix is permeable to the amine functional drug in free base form and the self adhesive matrix is substantially impermeable to the amine functional drug in protonated form.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Chien et al. is directed to transdermal controlled delivery of pharmaceuticals at variable dosage rates and processes. The transdermal dosage unit for administration of one or more pharmaceuticals at controlled and variable rates comprises a backing layer which is impervious to the ingredients of the dosage unit, a reservoir having present for transdermal absorption, a means which desirably provide variable transdermal absorption rates and an adhesive means to affix the dosage unit to the skin (column 2, lines 28-48). It is taught that if the at least one pharmaceutical is to be present in the reservoir in the form of microreservoirs of the pharmaceutical, the pharmaceutical can be dissolved in a biocompatible liquid which can provide variability of transdermal

absorption. The pharmaceutical can be dissolved or dispersed in the liquid before dispersion into a biocompatible polymeric material, such as an adhesive polymer and then stirred at sufficiently high speed to form a pharmaceutical containing polymeric material **wherein microreservoirs of the dissolved pharmaceutical are dispersed in a polymeric material** (column 4, lines 1-16). The backing layer can be made of any suitable material which is impermeable to the pharmaceutical dispersed within the adjacent reservoir layer (column 6, lines 33-35). Examples include a laminate of aluminum foil and polyester film (column 6, lines 64-66). The polymer material selected must permit the pharmaceutical to be released for the desired transdermal absorption and not substantially affect the pharmaceutical component or the permeability regulating membrane or other components. The reservoir medium containing dissolved/dispersed pharmaceutical and the polymeric material are combined in a suitable amount and agitated using suitable stirring or dispersing means to cause microreservoirs to be formed and homogeneously dispersed in the polymeric material. It is normally desired that the microreservoirs be of micronic diameter such as 2 to about 200 microns, usually preferably about 5 to 100 microns in diameter (column 9, lines 25-27). The adhesive polymer used can be selected from known adhesives which are bioacceptable and pressure sensitive (column 9, lines 28-40). The dosage units can vary in surface area and shape as desired (column 9, lines 50-57). A wide variety of pharmaceuticals are taught as being suitable. These include morphine and other narcotic analgesics. However, it is stated that it is contemplated that any pharmaceutical can be utilized by this invention (column 11, lines 14-63).

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

While Chien et al. teach that any pharmaceutical can be utilized; Chien et al. do not teach that the pharmaceutical is an aminotetraline compound. While Chien et al. teach that the polymer in which the pharmaceutical microreservoirs can be dispersed include adhesives, Chien et al. do not specify that the adhesive is a silicone adhesive. However, these deficiencies are cured by Muller al.

Muller et al. (where US Patent No. 6884434 is serving as the English Language equivalent of WO 99/49852) is directed to a transdermal therapeutic system which contains a D2 agonist. The device is utilized for the treatment of Parkinson's syndrome (column 1, lines 9-10). The matrix systems for drug delivery in their simplest forms consists of a backing layer, an active substance containing self-adhesive matrix and a protective film to be removed prior to use (column 2, lines 51-56). The adhesive system are either acrylate-based or silicone-based (column 2, lines 36-37). Silicone adhesives are in most cases polydimethylsiloxanes. However other organic residues may in principle be present instead of the methyl groups. The silicone adhesives are available as one component adhesives in two variants as so-called amine-resistant and as non-amine-resistant adhesives. Due to the basic nature of rotigotine (5,6,7,8-tetrahydro-6-[propyl-2[-(20thienyl)ethyl]amino-1-naphthalenol), silicone adhesives that are amine-resistant are used (column 3, lines 1-10). The adhesive's dissolving capacity of the active substance is an important parameter for the development of matrix systems (column 3, lines 15-17). It is taught that for silicone adhesives only the active substance base is suitable for use as salts thereof are practically insoluble in these types of

adhesives. Additionally it is taught that if polyvinylpyrrolidone is added to the adhesive, the dissolving capacity for the free base in such matrices is increased (column 3, lines 55-67). Auxiliary substances such as alkaline substances can be added a solution of the active substance in order to convert the active substance hydrochloride into the free active substance base. Then the solution may be filtered whereby the reactants with the exception of the active substance are eliminated (column 4, lines 28-48).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Chien et al. and Muller et al. and utilize rotigotine free base in the drug delivery device of Chien et al. One would have been motivated to utilize the rotigotine free base as Chien et al. teach that pretty much any pharmaceutical agent can be delivered. Muller et al. is directed to transdermal delivery systems comprising rotigotine which is a drug taught as treating Parkinson's disease. One of ordinary skill in the art would have been motivated to utilize the rotigotine free base when utilizing silicone adhesives as it is taught by Muller et al. that the free base or the hydrochloride salt which is converted to the free base are soluble whereas salts of the active substances are practically insoluble in these types of adhesives. Therefore, one of ordinary skill in the art would have been motivated to utilize rotogotine base when desiring to treat Parkinson's disease transdermally. Further more, the selection of a specific drug is considered prima facie obvious depending on the desired condition/symptoms to be treated.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Chien et al. and Muller et al. and utilize silicone adhesives. One of ordinary skill in the art would have been motivated to utilize silicone adhesives as Chien et al. teach that the adhesive polymer used can be selected from known adhesives which are bioacceptable and pressure sensitive. Muller et al. exemplify utilizing that amine resistant silicone adhesives with rotogotine dispersed therein. Therefore, one of ordinary skill in the art would have been motivated to utilize silicone adhesives as they are a known adhesive suitable for use with rotogotine base. The prior art teaches the use of rotogotine with silicone adhesives. Therefore, all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. **Note: MPEP 2141 [R-6]** *KSR International CO. v. Teleflex Inc.* 82 USPQ 2d 1385 (Supreme Court 2007).

Regarding the claimed limitation that the maximum diameter is less than the thickness of the self-adhesive matrix, it is taught that the microreservoirs are dispersed in the polymeric adhesive. Since they are dispersed therein, their corresponding diameter would be less than the thickness of the adhesive matrix. Furthermore, the method of making the microreservoirs are substantially similar to the method taught in the instant specification.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. in view of Gale et al. and in further view of Pfister et al. (US Patent No. 5232702, cited in the Office action mailed on 2/2/09).

Applicant Claims

The instant application claims the polymer matrix comprises two or more silicone pressure sensitive adhesives. The instant application claims the silicone pressure sensitive adhesive is a blend of a high tack silicone pressure sensitive adhesive comprising polysiloxane with a resin and medium tack silicone pressure sensitive adhesive comprising polysiloxane with a resin.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Chien et al. and Gale et al. are set forth above. Chien et al. is directed to a transdermal drug delivery system comprising microreservoirs. Gale et al. teach utilizing silicone adhesives in transdermal patches with the free base of fentanyl.

Ascertainment of the Difference Between Scope of the Prior Art and the Claims *(MPEP §2141.012)*

Chien et al do not teach utilizing a blend of high tack and medium tack silicone pressure sensitive adhesives. However, this deficiency is cured by Pfister et al.

Pfister et al. is directed to silicone pressure sensitive adhesive compositions for transdermal drug delivery. Example B (column 13) teach that an adhesive formulation consisting of a low silanol containing amine compatible silicone adhesive (Adhesive II) and a high silanol containing silicone adhesive (adhesive I) were prepared. The compositions were evaluated for flow reduction and creep resistance. It is taught that adhesive II has lower cohesive strength and exhibits significantly more flow when compared to adhesive I, which in many cases this is a disadvantage where an amine compatible adhesive is required. However, by combining adhesive I and adhesive II, a significant reduction of flow and improved creep resistance was achieved.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Chien et al., Gale et al. and Pfister et al. and utilize a combination of a low silanol containing amine-compatible silicone adhesive and a high silanol containing silicone adhesive. One of ordinary skill in the art would have been motivated to utilize this combination as it is taught by Pfister et al. as providing an adhesive with significant reduction of flow and improved creep resistance where amine-compatible adhesives are required. As taught by Gale et al. when utilizing a basic drug such as fentanyl, amine-resistant adhesive are used. Therefore, one of

ordinary skill in the art would have been motivated to utilize this mixture in order to provide an adhesive with significant reduction of flow and improved creep resistance.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. in view of Gale et al. and in further view of Lipp et al. (US Patent No. 5676968, cited in the Office action mailed on 4/27/10).

Applicant Claims

The instant application claims the microreservoirs further contain at least one crystallization inhibitor. A specific inhibitor claimed is polyvinylpyrrolidone.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Chien et al. and Gale et al. are set forth above. Chien et al. is directed to a transdermal drug delivery system comprising microreservoirs. Gale et al. teach utilizing silicone adhesives in transdermal patches with the free base of fentanyl.

Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)

Chien et al do not teach utilizing a crystallization inhibitor. However, this deficiency is cured by Lipp et al.

Lipp et al. is directed to transdermal therapeutic systems with crystallization inhibitors. The crystallization inhibitors are contained in the active ingredient-containing matrix (column 1, lines 5-9). It is taught that to prevent the crystallization processes in transdermal therapeutic systems and to be able to administer the therapeutically desired dose continuously, crystallization inhibitors are added (column 1, lines 44-50). Examples of crystallization inhibitors include highly dispersed silicon dioxide or macromolecular substances. Examples of macromolecular substances include polyvinylpyrrolidones. Polyvinylpyrrolidones and their copolymers with vinyl acetate and highly dispersed silicone dioxide are distinguished by a high crystallization-inhibitory potency (columns 1-2, lines 66-67 and 1-18). It is taught that crystallization inhibitors can be used in all known transdermal systems (column 2, lines 19-20).

Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Chien et al., Gale et al. and Lipp et al. and utilize a crystallization inhibitor in the microreservoir. One of ordinary skill in the art would have been motivated to utilize a crystallization inhibitor such as polyvinylpyrrolidone as they are known to be utilized in transdermal systems to prevent

active agent crystal growth. Therefore, one of ordinary skill in the art would have been motivated to add a crystallization inhibitor as taught by Lipp et al. in order to prevent the crystallization of the active agent. One of ordinary skill in the art would have been motivated to utilize polyvinylpyrrolidone as it is a macromolecule known to posses a high crystallization inhibitory potency.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicants argue that (1) Chien does not make any differentiation of drugs in free base form versus and protonated form. Chien is not enabling for all of the drugs mentioned. Applicants argue that (2) neither Chien nor Gale teaches that the microreservoirs should be less than the thickness of the matrix. Applicants argue just because the microreservoirs are dispersed in a matrix does not mean that their maximum diameter is less than the thickness of the matrix. Applicants argue that (3) the self-adhesive matrix is substantially impermeable to the amine functional drug in protonated form and the matrix functions as both adhesive and permeability control.

Applicants' arguments filed October 27 2010 have been fully considered but they are not persuasive.

Regarding applicants' first argument, there are two forms of drug (free base or salt form). Chien et al. clearly indicates some of the drugs are in salt form where as others are not listed in salt form therefore they can be reasonably interpreted as being in free base form. Gale clearly contemplates the use of fentanyl in free base form (claim 21). Therefore when using this drug in the drug delivery device of Chien et al., the examiner maintains that based on the teachings of Gale the free base form of fentanyl would have been obvious. While applicants' feel that Gale is not enabling for all the drugs listed, no evidence has been put forth that persuasively shows this. While applicants argue that the examples and the claims of Chien are only directed to hormones. Firstly the rejection is made under 103 and does not need to exemplify all embodiments, only suggest. "Disclosed examples and preferred embodiments do not constitute a teaching away from the broader disclosure or non-preferred embodiment." *In re Susi,* 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Furthermore, the examiner directs applicant's attention to MPEP 2121: PRIOR ART IS PRESUMED TO OPERABLE/ENABLING. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). Also see MPEP 716.07. The examiner further points to MPEP 2121.01 (II): "Even if a reference discloses an inoperative device, it is prior art for all that it teaches." Clearly, Chien teaches that a variety of other drugs can be utilized besides the exemplified hormones. Applicants have not shown that the other drugs taught by Chien would not work. While Chien may not recognize the same problem that Applicant's are attempting to solve, this is not the sole requirement for establishment of

a *prima facie* case of obviousness. Applicants' are directed to MPEP 2141: "It is not necessary in order to establish a *prima facie* case of obviousness that both a structural similarity between a claimed and prior art compound (or a key component of a composition) be shown and that there be a suggestion in or expectation from the prior art that the compound or composition will have the same or similar unity as one newly discovered by applicant". Chien clearly states that the listing of pharmaceuticals is merely exemplary and it is contemplated that any pharmaceutical can be utilized. Therefore, it would have been obvious to one of ordinary skill in the art to utilize other drugs which are known to be utilized in transdermal delivery such as rotigotine and fentanyl base with adhesive known to be suitable with these drugs such as silicone adhesives. While the term analgesic is broad term, the examiner still maintains one of ordinary skill in the art would have been motivated to select any analgesic, especially those already known to be delivered transdermally. Furthermore, applicants have not demonstrated the unobviousness of the specifically claimed analgesic. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Clearly Chien suggests the use of microreservoirs, an adhesive polymer and a drug. Gale and Muller suggest specific drug and adhesive combinations. Therefore, the examiner maintains the claimed transdermal delivery system is obvious.

Regarding applicants' second argument, the examiner disagrees. Thee examiner maintains that since the microreservoirs are dispersed in a matrix that their diameter is less than the thickness. Just because they may come to the edge of the matrix doesn't mean that they wouldn't have diameters less than the matrix. Clearly, the picture shown in Chien (Fig. 1) depicts the reservoirs being smaller than the total thickness of the matrix. Furthermore, those reservoirs coming to the edge of the matrix isn't excluded by the claims. Applicants' have not shown that the microreservoirs are not bigger than the thickness of the matrix

Regarding applicants' third argument, first a permeability control is not excluded from the claims. Applicants comprising language allows for other things to be present in the delivery system. Secondly, the examiner maintains it would have been obvious to utilize silicone adhesives. One of ordinary skill in the art would have been motivated to utilize silicone adhesives as Chien et al. teach that the adhesive polymer used can be selected from known adhesives which are bioacceptable and pressure sensitive. Muller et al. exemplify utilizing that amine resistant silicone adhesives with rotogotine dispersed therein. Gale et al. exemplify utilizing amine resistant silicone adhesives with fentanyl dispersed therein. Therefore, one of ordinary skill in the art would have been motivated to utilize silicone adhesives as they are a known adhesive suitable for use with fentanyl base or rotogotine. Since applicants claim the adhesive is a silicone pressure sensitive adhesive and that is what is taught by Gale and Mueller, their use would have been obvious. Applicants have not clearly established the unexpectedness of this particular adhesive.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
Examiner
Art Unit 1616

AF

/Mina Haghighatian/
Primary Examiner, Art Unit 1616